Deep annotation of mouse iso-miR and iso-moR variation.

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Public Summary:
With a dataset of more than 600 million small RNAs deeply sequenced from mouse hippocampal and staged sets of mouse cells that underwent reprogramming to induced pluripotent stem cells, we annotated the stem-loop precursors of the known miRNAs to identify isomoRs (miRNA-offset RNAs), loops, non-preferred strands, and guide strands. Products from both strands were readily detectable for most miRNAs. Changes in the dominant isomiR occurred among the cell types, as did switches of the preferred strand. The terminal nucleotide of the dominant isomiR aligned well with the dominant off-set sequence suggesting that Drosha cleavage generates most miRNA reads without terminal modification. Among the terminal modifications detected, most were non-templated mono- or di-nucleotide additions to the 3'-end. Based on the relative enrichment or depletion of specific nucleotide additions in an Ago-IP fraction there may be differential effects of these modifications on RISC loading. Sequence variation of the two strands at their cleavage sites suggested higher fidelity of Drosha than Dicer. These studies demonstrated multiple patterns of miRNA processing and considerable versatility in miRNA target selection.

Scientific Abstract:
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